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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS : Egan et al.
SERIAL NUMBER : 10/038,112 EXAMINER : Michel Graffeo
FILING DATE : December 31, 2001 ART UNIT : 1614
FOR : METHODS FOR TREATING GLAUCOMA IC

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION OF HOWARD B. HAIMES UNDER 37 C.F.R. §1.132

I, Howard B. Haimes, of 114 Woodland Street, Natick, MA, declare and state that:

1. I received Ph.D. degree in Biochemical Cytology from Sue Golding Graduate Division of the Albert Einstein College of Medicine, Yeshiva University, Bronx, NY and a M.S. in Biochemical Cytology from Sue Golding Graduate Division of the Albert Einstein College of Medicine, Yeshiva University, Bronx, NY and an M.S. degree in Biology from Long Island University, Brooklyn, NY and a B.S degree in Biology from Union College, Schenectady, NY .

2. I am presently employed by Alteon Inc., 221 West Grand Avenue, Suite 200, Montvale, NJ 07645, the assignee of the above-referenced patent application. I have been employed by Alteon Inc. for three years.

3. I have reviewed the Final Office Action dated January 24, 2007. I understand that claims 1, 2, 4, 8, 9, 11 and 13-17 over RE38,330 to Cerami ("Cerami") in view of U.S. Patent 5,153,205 to Lotti ("Lotti").

4. I have reviewed the present application in conjunction with the Cerami and Lotti references.

5. I disagree with the Examiner's assertion it would be obvious to combine the thiazolium compounds of Cerami with the cholinergic agents of Lotti to decrease intraocular pressure or improve ocular accommodation.

6. The eye constantly produces aqueous humor, the clear fluid that fills the anterior chamber (the space between the cornea and iris). The aqueous humor filters out of the anterior chamber through a complex drainage system. The delicate balance between the production and drainage of aqueous humor determines the intraocular pressure. Normal human intraocular pressure ranges between 8mm and 21mm Hg. Increased intraocular pressure indicates a problem with the amount of aqueous humor in the eye: either the eye is producing too much, or it's not draining properly. High intraocular pressure is a major risk factor for glaucoma. Glaucoma is an eye disorder that causes progressive and irreversible optic nerve damage and vision loss.

   Although not everyone with intraocular pressure above 20mm Hg develops glaucoma, someone with the pressure over 20mm Hg is more likely to develop glaucoma than someone with a lower pressure. Also, there are some people who have an intraocular pressure below 20mm Hg who develop glaucoma, this is called normal tension glaucoma.

   Depending on the type of glaucoma, various symptoms may be experienced. There is gradual loss of peripheral vision and night vision. Blurred vision and colored rings around lights accompany these symptoms. If intraocular pressure remains high, tunnel vision can develop.

   Glaucoma Risk factors include age, race (African-Americans and persons of Japanese decent have a higher incidence of glaucoma), sex (females are high risk), family history and medical disorders (*e.g.*, presence of hyperopia or farsightedness, diabetes or previous eye injury). Although glaucoma cannot be cured, in most cases it can be successfully controlled. Glaucoma treatment entails decreasing aqueous humor production, increasing fluid drainage or a combination of the two, thereby decreasing intraocular pressure. Intraocular pressure treatment may be in the form of medication (*e.g.*, eye drops containing beta-blockers or alpha-2 agonists), laser therapy or surgery (*e.g.*, trabeculoplasty, trabeculectomy).

7. Diabetic retinopathy is a disorder of the retinal blood vessels resulting from diabetes. Everyone who has diabetes is at risk for developing diabetic retinopathy, but not all diabetics do develop it. The incidence of diabetic retinopathy increases with the duration of diabetes. About 60% of patients having diabetes for 15 years or more will have some blood vessel damage in their eyes and a percentage of these are at risk of developing blindness. Patients with diabetic retinopathy are also at a greater risk of developing retinal tears and detachment.

   In diabetic retinopathy, the small blood vessels that are in the retina are damaged and become leaky. New blood vessels can also grow in the back of the eye. These new vessels are abnormal and bleed easily, sometimes filing the back of the eye with blood. This causes the retina to swell and form deposits. The affect of diabetic retinopathy on vision varies widely, depending on the stage of the disease. Some common symptoms include blurred vision, floaters and flashes and sudden vision loss. Risk factors for diabetic retinopathy include high blood glucose, poor diet and lack of exercise.

   Diabetic retinopathy is treated in many ways, depending on the stage of the disease and the specific problem that requires attention. The preferred method of treatment is laser photocoagulation to seal off leaking blood vessels and destroy new growth or in more extensive cases, vitrectomy. Many patients control their diabetes with diet and medication to delay or prevent the development of diabetic retinopathy and other complications.

   Although diabetes and diabetic retinopathy are risk factors for increased intraocular pressure and glaucoma, not all diabetics or people suffering from diabetic retinopathy develop increased intraocular pressure or glaucoma. In fact, while most diabetics develop diabetic retinopathy over time, the same cannot be said for intraocular pressure and/or glaucoma. Specifically, the instant specification teaches that primary open angle glaucoma (the predominant form of glaucoma) occurs in approximately 4% of diabetics compared to 1.8% of the general population. *See*, page 1, lines 18-32.

8. Cataracts are a disorder characterized by a clouding of the eye's natural lens, which lies behind the iris and the pupil. The lens is mostly made of water and protein. The protein is arranged in a precise way that keeps the lens clear and lets light pass through it. But as people age, some of the protein may clump together and start to cloud a small area of the

lens. This is a cataract, and over time, it may grow larger and cloud more of the lens, making it harder to see. Cataracts are classified as one of three types: nuclear, cortical or subcapsular. The type of cataract you have will affect exactly which symptoms you experience and how soon they will occur.

In general, it is not clear why the eye's lens changes over time, forming cataracts; however, risk factors include exposure to ultraviolet light or other forms of radiation, cigarette smoke, air pollution, heavy alcohol consumption, diet high in salt, diabetes and the use of steroids, diuretics and major tranquilizers

When symptoms begin to appear, vision may be improved temporarily using new glasses, strong bifocals, magnification, appropriate lighting or other visual aids. However, cataract surgery, which involves the replacement of the clouded lens with a clear, plastic intraocular lens, is recommended for most cataract sufferers and is very successful in restoring vision.

Cataracts are a separate disorder, unrelated to glaucoma or increase intraocular pressure. The only relation between cataracts and glaucoma or increase intraocular pressure is that these disorders share diabetes as one risk factor.

9. I assert that one of ordinary skill in the art would readily recognize that the etiology, symptoms and treatment of glaucoma/increased intraocular pressure is quite different from that of diabetic retinopathy or cataracts and would further recognize that while diabetics are twice as likely to develop glaucoma as compared to the general population, glaucoma/increased intraocular pressure is not a natural consequence that necessarily flows from diabetes, diabetic retinopathy or cataracts.

10. I further declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. § 1001 and that willful false statements may jeopardize the validity of this application and any patent issuing therefrom.

Howard B. Haimes

Signed at Montvale, NJ

this 12th day of March, 2007

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